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Iqbal Malik, Editor

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ISCHAEMIC HEART DISEASE

More proof that use of the correct medication saves lives in ACS ► Data from the > 20 000 patients in the GRACE registry of acute coronary syndromes (ACS) suggests several important take-home messages. This study focused on quality of care. Use of medications in eligible patients at discharge ranged from 73% for angiotensin converting enzyme (ACE) inhibitors to 93% for aspirin. High risk features (for example, heart failure, older age) were related to failure to use aspirin and β blockers. Being treated at a teaching hospital and care by a cardiologist were associated with greater use of aspirin and β blockers. Coronary artery bypass surgery (CABG) was associated with failure to use ACE inhibitors and aspirin. When hospitals were divided into quartiles of quality performance, adjusted in-hospital mortality was 4.1% in the top versus 5.6% in the bottom quartile, representing a 27% (95% confidence interval (CI) 11% to 42%) lower relative mortality. So, special care to ensure appropriate use of medical treatments seems warranted, especially for patients looked after in smaller hospitals, cared for by non-cardiologists, or having CABG.

▲ Granger CB, Steg PG, Peterson E, *et al*. Medication performance measures and mortality following acute coronary syndromes. *Am J Med* 2005;**118**:858–65.

Pre-treatment with clopidogrel after thrombolysis reduces risk from PCI ► In PCI-CLARITY, > 1800 patients received aspirin and were randomised to receive either clopidogrel (300 mg loading dose, then 75 mg once daily) or placebo initiated with fibrinolysis and given until coronary angiography, which was performed 2–8 days after initiation of the study drug. For patients undergoing coronary artery stenting, it was recommended that open label clopidogrel (including a loading dose) be administered after the diagnostic angiogram. The primary outcome was the incidence of the composite of cardiovascular death, recurrent myocardial infarction (MI), or stroke from percutaneous coronary intervention (PCI) to 30 days after randomisation. Secondary outcomes included MI or stroke before PCI and the aforementioned composite from randomisation to 30 days. Pretreatment with clopidogrel reduced the incidence of MI or stroke before PCI (37 (4.0%) *v* 58 (6.2%); odds ratio (OR) 0.62, 95% CI 0.40 to 0.95; p = 0.03). Overall, pretreatment with clopidogrel resulted in a highly significant reduction in cardiovascular death, MI, or stroke from randomisation through 30 days (70 (7.5%) *v* 112 (12.0%); adjusted OR 0.59, 95% CI 0.43 to 0.81; p = 0.001; number needed to treat = 23). There was no significant excess in the rates of TIMI (thrombolysis in myocardial infarction) major or minor bleeding (18 (2.0%) *v* 17 (1.9%); p > 0.99). Thus, clopidogrel should be part of the treatment regimen for all ACS patients.

▲ Sabatine MS, Cannon CP, Gibson CM, *et al* for the Clopidogrel as Adjunctive Reperfusion Therapy (CLARITY)–Thrombolysis in Myocardial Infarction (TIMI) 28 Investigators. Effect of clopidogrel pretreatment before percutaneous coronary intervention in patients with ST-elevation myocardial infarction treated with fibrinolytics: the PCI-CLARITY study. *JAMA* 2005;**294**:1224–32.

Presenting to hospital with ST elevation MI out of hours is dangerous ► Magid and colleagues used data from patients enrolled in the national registry of myocardial infarction (NRMI) between 1999 and 2002; 68 439 were treated with fibrinolytic therapy and 33 647 treated with PCI. Patient hospital arrival period was divided into regular hours (weekdays, 7 am to 5 pm) and off-hours (all other times). The majority of patients were treated outside of regular hours (67.9% of patients receiving fibrinolytic therapy, and 54.2% of PCI patients). Door-to-needle times were slightly longer during off hours (34.3 mins *v* 33.2 mins; p < 0.001), but door-to-balloon times were substantially longer during off-hours (116.1 mins *v* 94.8 mins; p < 0.001). The longer off-hours door-to-balloon times were mostly due to a longer interval between obtaining the ECG and patient arrival in the catheterisation laboratory (69.8 mins on average off-hours *v* 49.1 mins during regular hours; p < 0.001). Overall patients presenting during off-hours had higher adjusted in-hospital mortality than patients presenting during regular hours (OR 1.07; p = 0.02).

▲ Magid DJ, Wang Y, Herrin J, *et al*. Relationship between time of day, day of week, timeliness of reperfusion, and in-hospital mortality for patients with acute ST-segment elevation myocardial infarction. *JAMA* 2005;**294**:803–12.

Moving drug eluting stents into more complicated lesion types: it works ► Previous trials have proven that drug eluting stents (DES) improve outcome in simple lesion types. Now this trial suggests that this is true with more ''real life'' lesions. Compared with bare metal stents, paclitaxel eluting stents reduced the nine month rate of target lesion revascularisation from 15.7% to 8.6% (p < 0.001) and target vessel revascularisation from 17.3% to 12.1% (p = 0.02). Similar rates were observed for cardiac death or MI (5.5% for bare metal stent group *v* 5.7% for paclitaxel eluting stent group) and stent thrombosis (0.7% in both groups). Angiographic restenosis was reduced from 33.9% to 18.9% in the entire study cohort (p < 0.001), including among patients receiving 2.25 mm stents (49.4% *v* 31.2%; p = 0.01), 4.0 mm stents (14.4% *v* 3.5%; p = 0.02), and multiple stents (57.8% *v* 27.2%; p < 0.001).

▲ Stone GW, Ellis SG, Cannon L, *et al*, for the TAXUS V Investigators. Comparison of a polymer-based paclitaxel-eluting stent with a bare metal stent in patients with complex coronary artery disease: a randomized controlled trial. *JAMA* 2005;**294**:1215–23.

Are all drug coated stents equal? ► DES are better than bare metal stents in terms of restenosis. The two main available DES (Taxus using paclitaxel, and Cypher using sirolimus) have been considered about equal in terms of efficacy and safety. However, a meta-analysis of six trials, involving 3669 patients, showed that restenosis on angiography was less frequently observed among patients assigned to a sirolimus eluting stent (9.3%) versus a paclitaxel eluting stent (13.1%) (OR 0.68; p = 0.001). Event rates for sirolimus eluting versus paclitaxel eluting stents were, respectively, 0.9% and 1.1% for stent thrombosis, 1.4% and 1.6% for death, and 4.9% and 5.8% for death or MI. Target lesion revascularisation, the primary outcome of interest, was less frequently performed in patients who were treated with the sirolimus eluting stent (5.1%) versus the paclitaxel eluting stent (7.8%) (OR 0.64; p = 0.001) at 6–12 months.

▲ Kastrati A, Dibra A, Eberle SE, *et al*. Sirolimus-eluting vs paclitaxel-eluting stents in patients with coronary artery disease. *JAMA* 2005;**294**:819–25.

Sirolimus may be better than paclitaxel in preventing coronary restenosis ► In the trial reported by Windecker *et al*, with 1012 patients and using a composite primary end point of death from cardiac causes, MI, and ischaemia driven target lesion revascularisation at nine months, there were fewer events with sirolimus eluting stents (SS) than with paclitaxel eluting stents (PS) (6.2% *v* 10.8%), mainly as a result of a lower rate of target lesion revascularisation in the group with SS (4.8% *v* 8.3%). There also was less in-segment late luminal loss, the prespecified end point of the angiographic substudy, with SS than with PS (0.19 mm *v* 0.32 mm). During a similar interval, the ISAR-DIABETES investigators enrolled 250 patients with diabetes, a PCI cohort known to be at particularly high risk for restenosis as defined in both angiographic and clinical assessments. The study's primary end point of in-segment late luminal loss was measured by computer assisted quantitative angiography and revealed that there was less late loss with SS than with PS (0.43 mm *v* 0.67 mm). The corresponding rates of target lesion revascularisation were 6.4% and 12.0% (p = 0.13). Though not of adequate power to assess specific end points related to ischemia, such as death, MI, and stent thrombosis, neither trial observed a difference in these outcomes. In REALITY, with 1353 patients and 92% angiographic follow up,

greater late loss was observed in the group that had paclitaxel eluting stents, but this loss was not associated with a higher rate of target lesion revascularisation. Why the difference between SS and PS? These differences may lie in the underlying stent, the drug delivery polymer, and the antiproliferative agent. Although both stents have a closed cell design, they differ in cell geometry and strut thickness.

▲ Windecker S, Remondino A, Eberli FR, *et al*. Sirolimus-eluting and paclitaxel-eluting stents for coronary revascularization. *N Engl J Med* 2005;**353**:653–62.

▲ Dibra A, Kastrati A, Mehilli J, *et al*. Paclitaxel-eluting or sirolimus-eluting stents to prevent restenosis in diabetic patients. *N Engl J Med* 2005;**353**:663–70.

▲ Morice M-C, Serruys PW, Colombo A, *et al*. Eight-month outcome of the REALITY study: a prospective, randomized, multi-center head-to-head comparison of the sirolimus-eluting stent (Cypher) and the paclitaxel-eluting stent (Taxus). Orlando, Florida: Presented at the 2005 Annual Scientific Session of the American College of Cardiology, March 6–9, 2005.

GENERAL CARDIOLOGY

ECG interpretation by non-cardiologists in ER ► In a test of ECG interpretation, 120 doctors working in the emergency room (ER) or as internal medicine residents were given 12 ECGs. The median proficiency was 6 out of 10, total ECG score was 15 of 24, and certainty was 33 of 48. There was no significant difference in overall competency between emergency medicine and internal medicine residents (14.0 *v* 15.0; p = 0.239). Internal medicine residents interested in a cardiology career scored higher than those not interested in a cardiology career (17.3 *v* 14.1; p = 0.003). When analysing the most critical diagnoses, the mean score for ventricular tachycardia was 1.6 of 2.0, for MI was 1.3 of 2.0, and for complete heart block was 0.8 of 2.0. Over half of the participants felt their ECG training was inadequate.

▲ Berger JS, Eisen L, Nozad V, *et al*. Competency in electrocardiogram interpretation among internal medicine and emergency medicine residents. *Am J Med* 2005;**118**:873–80.

Internet based learning is as good as live interaction ► No one has tested internet based CME programs versus live courses. This trial compared a cholesterol guideline package delivered in these two ways and assessed long term outcomes. Knowledge was assessed immediately before the intervention, immediately after the intervention, and 12 weeks later. The percentage of high risk patients who had appropriate lipid panel screening and pharmacotherapeutic treatment according to guidelines was documented with chart audits conducted over a five month period before intervention and a five month period after intervention. Both interventions produced similar and significant immediate and 12 week knowledge gains, representing large increases in percentage of items correct (pre-test to post-test 31.0%; pre-test to 12 weeks 36.4%; $p < 0.001$ for all comparisons). Chart audits revealed high baseline screening rates in all patient groups (93%) with no significant post-intervention change. However, the internet based intervention was associated with a significant increase in the percentage of high risk patients treated with pharmacotherapeutics according to guidelines (pre-intervention 85.3%; post-intervention 90.3%; p = 0.04).

▲ Fordis M, King JE, Ballantyne CM, *et al*. Comparison of the instructional efficacy of internet-based CME with live interactive CME workshops: a randomized controlled trial. *JAMA* 2005;**294**:1043–51.

Primary prevention is more effective than secondary ► Modelling can be used to attribute mortality to certain factors. Between 1981 and 2000, CHD mortality rates fell by 54%, resulting in 68 230 fewer deaths in 2000. Overall smoking prevalence declined by 35% between 1981 and 2000, resulting in approximately 29 715 (minimum estimate 20 035, maximum estimate 44 675) fewer deaths attributable to smoking cessation: approximately 5035 in known CHD patients and approximately 24 680 in healthy people. Population total cholesterol concentrations fell by 4.2%, resulting in approximately 5770 fewer deaths attributable to dietary changes (1205 in CHD patients and 4565 in healthy people) plus 2135 fewer deaths attributable to statin treatment (1990 in CHD patients, 145 in people without CHD). Mean population blood pressure fell by 7.7%, resulting in approximately 5870 fewer deaths attributable to secular falls in blood pressure (520 in CHD patients and 5345 in healthy people) plus approximately 1890 fewer deaths attributable to antihypertensive treatments in people without CHD. Approximately 45 370 fewer deaths were thus attributable to reductions in the three major risk factors in the population: some 36 625 (81%) in people without recognised CHD and 8745 (19%) in CHD patients. Compared with secondary prevention, primary prevention achieved a fourfold larger reduction in deaths. Future CHD policies should prioritise population-wide tobacco control and healthier diets.

▲ Unal B, Critchley JA, Capewell S. Modelling the decline in coronary heart disease deaths in England and Wales, 1981–2000: comparing contributions from primary prevention and secondary prevention. *BMJ* 2005;**331**:614.

Regular contact with heart failure patients reduces readmissions ► A total of 1518 outpatients with stable chronic heart failure and optimal drug treatment, stratified by attending cardiologists, were randomised to telephone intervention or usual care. Education, counselling, and monitoring were provided by nurses through frequent telephone follow up in addition to usual care, delivered from a single centre. Complete follow up was available in 99.5% of patients. The 758 patients in the usual care group were more likely to be admitted for worsening heart failure or to die (235 events, 31%) than the 760 patients who received the telephone intervention (200 events, 26.3%) (relative risk reduction (RRR) 20%, 95% CI 3% to 34%; p = 0.026). This benefit was mostly due to a significant reduction in admissions for heart failure (RRR 29%; p = 0.005). Mortality was similar in both groups. At the end of the study the intervention group had a better quality of life than the usual care group (mean total score on Minnesota living with heart failure questionnaire 30.6 *v* 35; p = 0.001).

▲ GESICA Investigators. Randomised trial of telephone intervention in chronic heart failure: DIAL trial. *BMJ* 2005;**331**:425.

BASIC SCIENCE

Mouse cell transplantation to help injured hearts ► The ability to direct differentiation of embryonic stem cells (ESC) towards a cardiomyogenic phenotype makes them an attractive therapeutic option for cardiac repair, but species specific and individual specific immunological imprinting remains a hurdle. Engraftment and differentiation of cardiac committed mouse ESC was studied in 18 sheep in which an MI had been induced; nine controls received medium and nine sheep (five of which were immunosuppressed) received ESC. The gain in myocardial function was measured by echocardiography one month after cell transplantation. Cardiac committed murine ESC engrafted in infarcted myocardium of immunosuppressed and immunocompetent sheep, and differentiated into mature cardiomyocytes that expressed connexins. Colonisation of the scar area by ESC was accompanied by a functional benefit of the damaged myocardium. Left ventricular ejection fraction deteriorated in the control group by a median of 9.9% (range −20% to 0.3%) relative to baseline (p = 0.011) whereas in the treated group it improved by 6.6% (−5.7% to 50.8%; comparison between groups p = 0.002). Although good news, this type of engraftment might also result in arrhythmic circuits being formed.

▲ Ménard C, Hagège AA, Agbulut O, *et al*. Transplantation of cardiac-committed mouse embryonic stem cells to infarcted sheep myocardium: a preclinical study. *Lancet* 2005;**366**:1005–12.

Journals scanned

American Journal of Medicine; American Journal of Physiology: Heart and Circulatory Physiology; Annals of Emergency Medicine; Annals of Thoracic Surgery; Archives of Internal Medicine; BMJ; Chest; European Journal of Cardiothoracic Surgery; Lancet; JAMA; Journal of Clinical Investigation; Journal of Diabetes and its Complications; Journal of Immunology; Journal of Thoracic and Cardiovascular Surgery; Nature Medicine; New England Journal of Medicine; Pharmacoeconomics; Thorax

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